

**ABSTRACT:**

This invention relates to modified pneumolysin polypeptides that retain the immunogenic nature of pneumolysin but have reduced or undetectable hemolytic activity compared to native pneumolysin. The invention also provides a method for generating novel pneumolysin variants with these desired characteristic properties. The invention also provides immunogenic compositions useful as pharmaceutical compositions including vaccines in which non-toxic, modified pneumolysin is used to stimulate protective immunity against *Streptococcus pneumoniae*. The vaccines may be compositions in which the modified pneumolysin is conjugated to bacterial polysaccharides or may be carried on an attenuated viral vector. In addition, the invention also provides a method of using the non-toxic, modified pneumolysin toxoid in order to stimulate antibodies against *Streptococcus pneumoniae* in a treated individual which are then isolated and transferred to a second individual, thereby conferring protection against *Streptococcus pneumoniae* in the second individual.